#4

**REMARKS**

Applicants have added into the present specification a new paper copy Sequence Listing section according to 37 C.F.R. §1.821(c) as new pages 1-2, and have renumbered the subsequent pages accordingly. Furthermore, attached hereto is a 3 1/2" disk containing the "Sequence Listing" in computer readable form in accordance with 37 C.F.R. §1.821(e).

Applicants have amended the specification to insert SEQ ID Nos, as supported in the present specification.

The following statement is provided to meet the requirements of 37 C.F.R. §1.821(f) and 1.821(g).

I hereby state, in accordance with 37 C.F.R. §1.821(f), that the content of the attached paper and computer readable copies of the sequence listing are believed to be the same.

I hereby also state, in accordance with 37 C.F.R. §1.821(g), that the submission is not believed to include new matter.

Under U.S. rules, each sequence must be classified in <213> as an "Artificial Sequence", a sequence of "Unknown" origin, or a sequence originating in a particular organism, identified by its scientific name.

Neither the rules nor the MPEP clarify the nature of the relationship which must exist between a listed sequence and an organism for that organism to be identified as the origin of the sequence under <213>.

Hence, counsel may choose to identify a listed sequence as associated with a particular organism even though that sequence does not occur in nature by itself in that organism (it may be, e.g., an epitopic fragment of a naturally occurring protein, or a cDNA of a naturally occurring mRNA, or even a substitution mutant of a naturally occurring sequence). Hence, the identification of an organism in <213> should not be construed as an admission that the sequence *per se* occurs in nature in said organism.

Similarly, designation of a sequence as "artificial" should not be construed as a representation that the sequence has no association with any organism. For example, a primer or probe may be designated as "artificial" even though it is necessarily complementary to some target sequence, which may occur in nature. Or an "artificial" sequence may be a substitution mutant of a natural sequence, or a chimera of two or more natural sequences, or a cDNA (i.e., intron-free sequence) corresponding to an intron-containing gene, or otherwise a fragment of a natural sequence.

The Examiner should be able to judge the relationship of the enumerated sequences to natural sequences by giving full consideration to the specification, the art cited therein, any further art cited in an IDS, and the results of his or her sequence search against a database containing known natural sequences.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current

amendment. The attached page is captioned "Version with markings to show changes made".

Applicants submit that the present application contains patentable subject matter and therefore urge the examiner to pass the case to issuance.

If the examiner has any questions or comments concerning the above described application, the examiner is urged to contact the undersigned at the phone number below.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

The paragraph beginning at line 1 of page 11 has been amended as follows:

Fig 10 is a schematic drawing of PDGF-BB bound by two aptamer based proximity-probes, A1c (SEQ ID NO:1) and A2c (SEQ ID NO:2). The aptamer sequence which binds PDGF-BB is shown in close to the protein. The TaqMan probe sequence (reverse complement of SEQ ID NO:3) used in PCR detection is shown. The ligation junction between the proximity-probes is marked with a line between the 3´end of A1c and the 5′ end of A2c. The primer sites are boxed. The ligation template is SEQ ID NO:4.

The paragraph beginning at line 12 of page 13 has been amended as follows:

Probe A1c :
TACTCAGGGCACTGCAAGCAATTGTGGTCCCAATGGGCTGAGTATGTGGTCTATGTCGTCGT
TCGCTAGTAGTTCCTGGGCTGCAC (SEQ ID NO:1)
Probe A2c :
TCGAGGCGTAGAATTCCCCCGATGCGCGCTGTTCTTACTCAGGGCACTGCAAGCAATTGTGG
TCCCAATGGGCTGAGTAT (SEQ ID NO:2)
Splint template for ligation (6+20):
GGGGGAATTCTACGCCTCGAGTGCAG (SEQ ID NO:3)
Frw primer: ATGTGGTCTATGTCGTCGTTCG (nucleotides 44-65 of SEQ ID NO:1)
Rew primer: TGAGTAAGAACAGCGCGCAT (reverse complement of nucleotides 22-41 of SEQ ID NO:2)
Taq Man probe A1+2c: Fluor-CTGCACTCGAGGCGTAGAATTCCCC-Tamra (reverse complement of SEQ ID NO:3)

PCR cycles: hold 10 min 95, cycle 95 (15 sec) - 60 (1 min) 45 times